



# The EuroInf study: A multicentre European comparative case control study of apomorphine versus intrajejunal levodopa infusion in advanced Parkinson's disease

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On behalf of EUROPAR and the Movement Disorders Society Non Motor PD Study Group

## Background

Intrajejunal levodopa infusion (IJL) and subcutaneous apomorphine infusion (Apo) are established treatment for advanced Parkinson's disease (PD) although there are considerable differences in cost of treatment.

## Methods

- 87 patients with advanced PD were assessed with
- Unified PD Rating Scale (UPDRS) III and IV, Non Motor Symptoms Scale (NMSS), PDQ-8 (Quality of Life Questionnaire) scores
- before initiation of therapy and
- after 6 months of therapy.

Demo-graphics	Apo	IJL
Number of patients	n = 43	n = 44
Mean Age (yrs)	62.25 ±10.60	62.66 ±9.09
Mean duration of disease (yrs)	14.04 ±4.4	16.06 ±6.7
Median H&Y	Stage 3	Stage 3

## Results:

- Both groups were matched in terms of age, duration of PD, median HY stage, levodopa equivalence dose
- Effect size of both intervention on UPDRS III&IV and PDQ-8 scores were big (>0.8).
- Concerning the NMSS, differential effect was observed with sleep/fatigue and gastroenterological symptoms showing greater response to IJL, while mood was better improved with Apo with no worsening of hallucinations.

Baseline vs. Follow-up	Relative change (%)			Effect size	
	Apo	IJL	p*	Apo	IJL
UPDRS- Part 3	-43.26	-44.79	NS	1.28	1.00
UPDRS- Part 4	-40.84	-56.06	NS	0.87	1.69
<b>NMSS Domains</b>					
Cardiovascular	-35.11	-44.64	NS	0.25	0.41
Sleep/Fatigue	-23.56	-48.23	0.017	0.40	0.73
Mood/Apathy	-47.00	-24.75	0.030	0.49	0.30
Perceptual/Hallucinations	-53.97	-44.79	NS	0.32	0.29
Attention/Memory	-33.98	-25.60	NS	0.36	0.28
Gastrointestinal	-25.12	-55.17	0.004	0.27	0.68
Urinary	-12.57	-52.36	0.0001	0.15	0.58
Sexual functioning	-24.61	-59.51	0.001	0.12	0.43
Miscellaneous	-31.08	-33.97	NS	0.39	0.54
<b>NMSS Total score</b>	<b>-31.76</b>	<b>-41.01</b>	<b>NS</b>	<b>0.53</b>	<b>0.83</b>
<b>PDQ-8 Summary index</b>	<b>-29.75</b>	<b>-34.21</b>	<b>NS</b>	<b>0.89</b>	<b>1.14</b>

Effect size: 0.2-0.49: small, 0.5-0.79: medium, ≥ 0.8: large  
Moderate to large is desirable

## Objective

- Comparative data collection (motor and non motor effects) of Intrajejunal levodopa infusion (IJL) and subcutaneous apomorphine infusion (Apo)
- Reporting of multicentre European data from a real life case control study of cases with advanced PD.

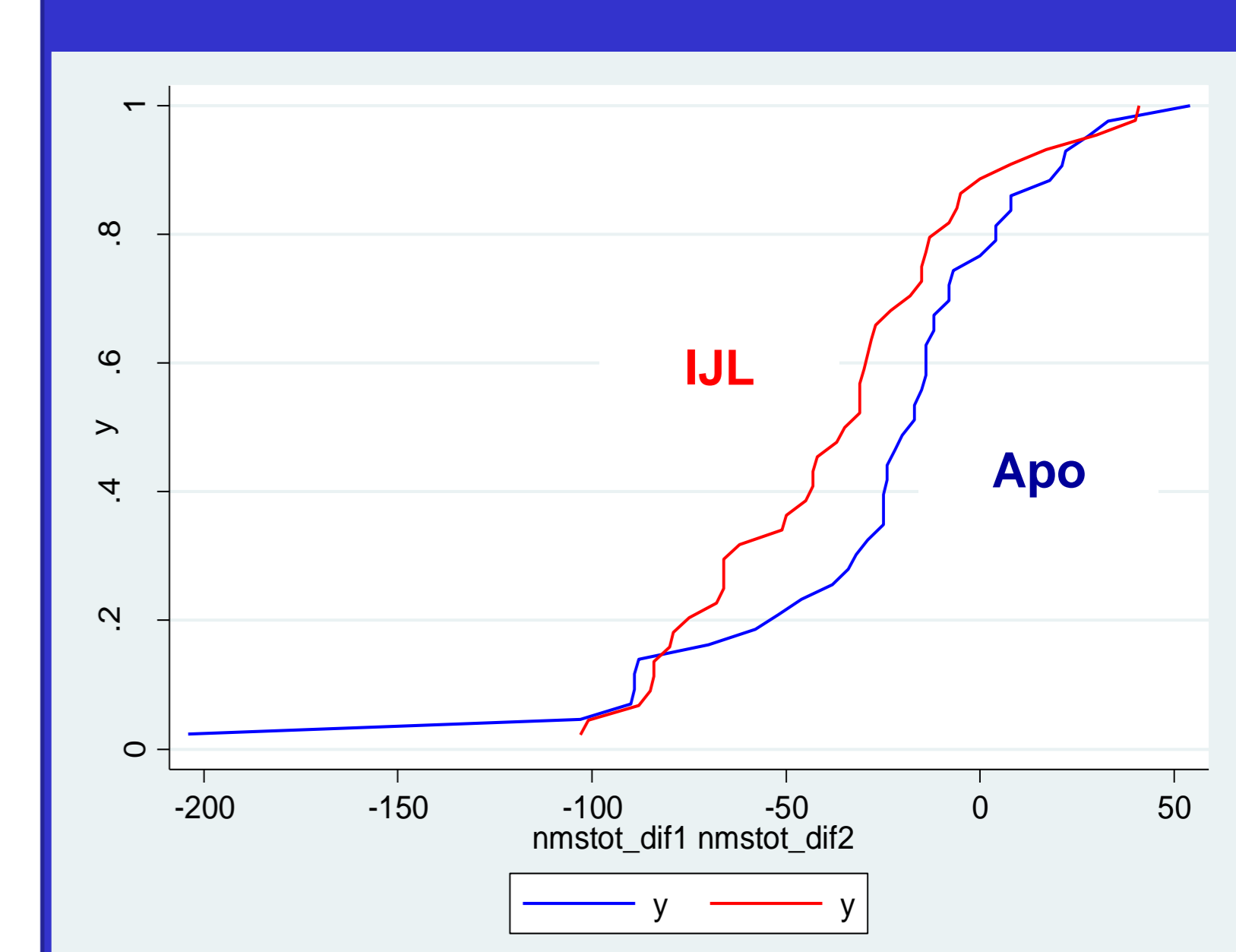
	Apomorphine					IJ Levodopa				
	Baseline		Follow-up		P*	Baseline		Follow-up		P*
	Mean	SD	Mean	SD		Mean	SD	Mean	SD	
UPDRS- Part 3	30.79	10.40	17.46	8.08	<0.0001	27.29	12.28	15.07	10.37	<0.0001
UPDRS- Part 4	10.02	4.68	5.93	3.35	<0.0001	9.93	3.29	4.36	3.07	<0.0001
<b>NMSS Domains</b>										
Cardiovascular	3.19	4.57	2.07	2.49	0.23	3.36	3.69	1.86	2.67	0.0076
Sleep/Fatigue	16.98	10.12	12.98	10.13	0.024	16.68	10.97	8.64	8.26	<0.0001
Mood/Apathy	18.81	18.00	9.98	10.17	0.0003	15.79	12.85	11.89	13.04	0.021
Hallucination	3.02	5.18	1.40	3.14	0.003	3.54	5.54	1.95	4.51	0.010
Attention/Memory	8.77	8.24	5.79	6.35	0.003	10.20	9.35	7.60	8.68	0.011
Gastrointestinal	6.21	5.82	4.65	5.49	0.003	9.48	7.68	4.25	4.80	<0.0001
Urinary	9.07	7.40	7.93	8.03	0.002	11.5	10.42	5.48	5.78	0.0001
Sexual functioning	2.56	5.29	1.93	3.59	0.18	5.73	7.93	2.32	4.12	0.014
Miscellaneous	13.77	10.94	9.49	8.15	0.50	14.66	9.25	9.68	7.87	0.0008
<b>NMSS Total score</b>	<b>82.37</b>	<b>49.54</b>	<b>56.21</b>	<b>32.21</b>	<b>0.0007</b>	<b>90.95</b>	<b>45.00</b>	<b>53.66</b>	<b>38.67</b>	<b>&lt;0.0001</b>
<b>PDQ-8 Summary index</b>	<b>49.85</b>	<b>16.59</b>	<b>35.03</b>	<b>18.00</b>	<b>&lt;0.0001</b>	<b>48.58</b>	<b>14.62</b>	<b>31.96</b>	<b>14.89</b>	<b>&lt;0.0001</b>

Correction of Benjamini-Hochberg for multiple comparisons: significant if p< 0.027

## Results effect size:

- Motor effect**  
Both Apo and IJLI have large effect on UPDRS 3 and 4 but trend towards greater effect of IJLI on UPDRS 4 (1.69 vs 0.87, p=NS)
- Non Motor effect:**
  - Sleep and fatigue: IJLI > Apo (0.73 vs 0.4, p= 0.017)
  - Mood and apathy: Apo > IJLI (0.49 vs 0.3, p= 0.03)
  - Autonomic (GIT/Urinary) IJLI >> Apo (Apo = small vs IJL = moderate effect)
  - Hallucinations: No worsening or reports with Apo or IJL
- Quality of life:**  
Large beneficial effect of Apo and IJL: (0.89 vs 1.14, p=NS)

## Cumulative distribution Function – NMS Scale Total Score



## Adverse Effects

Apo (n=43)	IJL (n=44)
Skin Nodules (none required discontinuation)	Demyelinating polyneuropathy x 3, discontinued x 2
Failure of therapy and IJLI/DBS started x 3	Severe weight loss/malabsorption syndrome x 7 (1 diagnosed CA colon)
Incident ICD x 2	No ICD's and ICD resolved in 4
Severe Somnolence x 2 (discontinuation x 1)	Tube detachment
	Peritonitis x 2, 1 death

## CONCLUSIONS:

- First head to head real life multicentre comparative study of Apo infusion vs. IJL in relatively matched advanced PD.
- Both Apo and IJL produce robust and significant improvement in motor and aspects of non motor functions in advanced PD and most importantly, quality of life.
- However there are differences:
  - IJL causes greater dyskinesia reduction and has significantly better effect on gastrointestinal and genitourinary dysfunction
  - IJL leads to resolution of pre-existing ICD in some cases
  - Apomorphine infusion has a greater effect on dysphoria and mood dysfunction and low rate of significant ICD development and no worsening or development of hallucinations/psychosis in the observation period.
  - Side effects with IJL need monitoring particularly: Demyelinating polyneuropathy (6.8%)  
Weight loss and malabsorption syndrome (15.9%)